

Tripple Negative Breast Cancer in Younger Population: Clinical Features and Prognostic Factors

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ARTICLE INFO

Received: 9 June 2026
Accepted: 15 June 2026
Published Online: 19 June 2026

DOI: 10.5281/zenodo.20760848

Volume: 9, Number: 4, Page: 211-215

e-ISSN: 2789-5912
ISSN: 2617-0817

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ABSTRACT

Background: Triple-negative breast cancer (TNBC) is a highly aggressive, basal-like type that does not express ER, PR, or HER2, leading to a poor outlook and elevated recurrence rates, particularly in women younger than 40. In Bangladesh, the primary treatment for invasive ductal carcinoma involves surgery and chemotherapy. This research explores clinical characteristics and prognostic indicators in younger TNBC patients to inform treatment decisions. **Methods & Materials:** A retrospective study conducted at Shikder Women's Medical College Hospital (July 2024–Dec 2025) involved women aged ≤ 40 years diagnosed with TNBC. Demographic data, tumor characteristics, molecular indicators, treatment details, and one-year relapse rates were examined using SPSS 26. Tumors were staged according to AJCC 8th edition, high Ki-67 $>40\%$, using Chi-square for associations ($p < 0.05$). Approval for ethical considerations was secured. **Results:** In 52 younger TNBC patients, the majority presented with T2, Grade III invasive ductal tumors, often accompanied by lymph node involvement and noticeable lumps. Elevated Ki-67 and p53 positivity were prevalent, with 25% showing positive results for BRCA1. The treatment encompassed surgery, chemotherapy, and radiotherapy, but did not involve hormonal or HER2 therapies. Early relapse was associated with greater tumor size, positive nodal involvement, high grade, and elevated Ki-67, but not with BRCA1 status. **Conclusion:** Younger patients with TNBC generally present with high-grade, invasive tumors that exhibit aggressive characteristics. Management involves surgery, chemotherapy, and radiotherapy, with early recurrence associated with significant tumor size, nodal involvement, high grade, and elevated Ki-67,

highlighting the necessity for attentive treatment.

Keywords: Tripple Negative Breast Cancer, Younger Population, Clinical Feature, Prognostic Factors.

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INTRODUCTION

Breast cancer is the most common cancer in women (23% of cases) and the leading cause of cancer death despite improved diagnosis and treatment [1,2,3]. It is divided into three categories: (1) ER (Estrogen Receptor)/PR (Progesterone Receptor)-positive (2) HER2(Human Epidermal Growth Factor Receptor2)-positive, and (3) triple-negative breast cancer (TNBC), which does not express ER, PR, or HER2. Targeted treatments are available for the first two categories, but none for TNBC [4]. Triple-negative breast cancers are characterized by the absence of estrogen receptor (ER), progesterone receptor (PR), and HER2 expression. Basal-like breast cancers represent one of the five distinct intrinsic subgroups of breast cancer, a finding uncovered through microarray expression profiling studies [5]. It accounts for 15–20% of breast cancers (approximately 170,000 cases). It is an aggressive, highly proliferative tumor and has the poorest prognosis among breast cancer subtypes [6,7,8]. It presents as a palpable breast lump, sometimes with skin changes, nipple abnormalities, or axillary lymph node enlargement, reflecting its aggressive nature [9]. Diagnosis of triple-negative breast cancer (TNBC) includes clinical

examination and imaging (mammography/ultrasound), validated by biopsy with immunohistochemistry indicating the lack of ER, PR, and HER2. Other indicators such as Ki-67 might help direct prognosis and therapy [10]. These cancers are typically less differentiated and frequently categorized as the basal subtype, marked by basal indicators like cytokeratin 5/6. Gene-expression profiling indicates they create a unique and fairly uniform transcriptional grouping [11]. Recent research shows that patients with triple-negative breast cancer often experience visceral metastases, such as to the brain, creating a clinically challenging problem and a primary area of current investigation [12,13]. The outlook for this tumor type is unfavorable, since hormonal treatment and trastuzumab show no effectiveness. Despite being a specific subgroup, mTNBC management adheres to standard metastatic breast cancer strategies, emphasizing the extension of survival and enhancement of quality of life via a tailored, patient-focused approach [14,15,16]. International research indicates that TNBC in females under 49 is more aggressive, associated with increased disease-specific mortality, and conventional prognostic factors are less reliable, emphasizing age as a distinct negative factor [17].

Patients with TNBC who are 35 years old or younger frequently show advanced, aggressive tumors, increased lymph node involvement, and expression of basal markers, resulting in a reduced disease-free survival [18]. Systematic reviews indicate that younger TNBC patients experience a higher risk of recurrence and reduced survival, positioning age at diagnosis as a crucial global prognostic factor [19]. The study by Akter et al. found that circulating tumor DNA (ctDNA) was detectable in all Bangladeshi TNBC patients, supporting its potential as a non-invasive biomarker for molecular analysis [20]. Another study by Tanjin et al. found that Bangladeshi TNBC patients were mostly in their early forties, multiparous, and often used contraceptives. Tumors were mainly invasive ductal carcinoma, grade II, frequently with lymph node involvement, and most patients received surgery and chemotherapy [21]. In Bangladesh, studies on TNBC among younger women are rare, with little information available regarding prognosis, recurrence, and risk factors. This research seeks to investigate the clinical characteristics and prognostic elements of TNBC in women younger than 40 to inform age-targeted treatment

METHODS & MATERIALS

This study was a hospital-based retrospective study conducted at Shikder Women’s Medical College Hospital. The study period spanned one and a half years, from July 2024 to December 2025. The study population included younger female patients (≤40 years) diagnosed with triple negative breast cancer (TNBC) who were treated or followed up at the hospital during the study period. Patients with incomplete medical records or insufficient follow-up data were excluded. Data were collected retrospectively from hospital medical records, pathology reports, and treatment files. Information obtained included socio-demographic characteristics (age, residence, occupation), clinical presentation (tumor size, lymph node status, clinical symptoms), histopathological and molecular features (histology type, grade,

Ki-67 proliferation index, p53 and BRCA1 status), treatment modalities (surgery, chemotherapy, radiotherapy), and early outcomes such as relapse within one year. Tumor staging and grading were recorded according to the AJCC (8th edition) TNM classification. High Ki-67 index was defined as >40%, and relapse within one year was considered an early prognostic event. Data were entered into a structured spreadsheet and analyzed using SPSS software (version 26.0). Descriptive statistics (frequency and percentage) were used to summarize categorical variables. Associations between prognostic factors and early relapse were assessed using the Chi-square test, with a p-value <0.05 considered statistically significant. The study was conducted after obtaining ethical approval from the Institutional

Ethical Review Committee, and confidentiality of patient records was strictly maintained throughout the study.

RESULTS

A total of 52 younger female patients (≤40 years) with triple negative breast cancer (TNBC) were included in this study. *Table I* shows the socio-demographic characteristics of the study population. The majority of patients were aged 31–35 years (34.6%), followed by 26–30 years (26.9%) and 36–40 years (26.9%). Most patients were from urban areas (59.6%), while 40.4% resided in rural areas. Regarding occupation, half of the participants were housewives (50%), followed by service holders (23.1%), students (11.5%), and business/other occupations (15.4%).

Table I
Socio-demographic characteristics of the study population (n = 52).

Characteristics	Frequency	Percentage (%)
Age group (years)		
20–25	6	11.5
26–30	14	26.9
31–35	18	34.6
36–40	14	26.9
Residence		
Urban	31	59.6
Rural	21	40.4
Occupation		
Housewife	26	50.0
Service holder	12	23.1
Student	6	11.5
Business/others	8	15.4

Table II presents the most common tumor size at presentation was T2 (2–5 cm) in 53.8%, followed by T3 (>5 cm) in 23.1%, T1 (<2 cm) in 11.5%, and T4 (chest wall/skin involvement) in 11.5% of cases. Lymph node involvement was observed in

the majority, with N1 (38.5%) and N2 (19.2%), while 30.8% had no nodal involvement (N0). High-grade tumors were prevalent, with Grade III tumors accounting for 57.7%, followed by Grade II (32.7%) and Grade I (9.7%). Clinically, the most

common presenting symptom was a palpable lump (92.3%), followed by pain (26.9%), skin changes such as peau d’orange or ulceration (15.4%), and nipple discharge (7.7%).

Table II
Clinical presentation of TNBC in younger patients (n = 52).

Clinical Feature	Frequency	Percentage (%)
Tumor size (T stage)		
T1 (<2 cm)	6	11.5
T2 (2–5 cm)	28	53.8
T3 (>5 cm)	12	23.1
T4 (chest wall/skin involvement)	6	11.5
Lymph node involvement (N stage)		
N0	16	30.8
N1	20	38.5
N2	10	19.2
N3	6	11.5
Histological grade		
Grade I	5	9.7
Grade II	17	32.7
Grade III	30	57.7
Clinical symptoms		
Palpable lump	48	92.3
Pain	14	26.9
Skin changes	8	15.4
Nipple discharge	4	7.7

Table III shows that invasive ductal carcinoma was the predominant histological type (92.3%), while medullary carcinoma and other subtypes were less common (5.8% and 1.9%, respectively). A high Ki-67 proliferation index (>40%) was observed in 65.4% of patients, indicating aggressive tumor biology. p53 positivity was present in 46.2% of patients. Among the subset tested for BRCA1 mutation (n = 20), 25% were positive.

Table III
Pathological and molecular features (n = 52).

Characteristics	Frequency	Percentage (%)
Histopathology type		
Invasive ductal carcinoma	48	92.3
Medullary carcinoma	3	5.8
Other	1	1.9
Ki-67 proliferation index		
<20%	4	7.7
20–40%	14	26.9
>40%	34	65.4
p53 mutation (IHC positive)	24	46.2
BRCA1 mutation (tested subset, n=20)	5	25.0

Table IV shows treatment modalities received by patients. The majority underwent surgery (86.5%) and received chemotherapy (98.1%), while radiotherapy was administered to 69.2%. As expected for TNBC, hormonal therapy and HER2-targeted therapy were not used.

Table IV
Treatment modalities received (n = 52).

Treatment	Frequency	Percentage (%)
Surgery	45	86.5
Chemotherapy (neo/adjuvant)	51	98.1
Radiotherapy	36	69.2
Hormonal therapy	0	0.0
Targeted therapy (HER2)	0	0.0

Table V presents during one-year follow-up, tumor size T3–T4 was significantly associated with early relapse (38.5% vs 22.2%; p = 0.042). Similarly, lymph node positivity (N1–N3) was strongly associated with relapse (69.2% vs 33.3%; p = 0.011). Patients with Grade III tumors and Ki-67 >40% also had significantly higher relapse rates (61.5% vs 38.9%; p = 0.029 and 69.2% vs 44.4%; p = 0.031, respectively). BRCA1 mutation status did not show a significant association with relapse (p = 0.91). These findings suggest that larger tumor size, nodal involvement, high histological grade, and elevated Ki-67 index are important predictors of early disease recurrence in younger TNBC patients.

Table V
Prognostic factors and early outcomes (n = 52).

Prognostic Factor	Relapse within 1 year	No relapse	p-value
Tumor size T3–T4	10 (38.5%)	8 (22.2%)	0.042*
Lymph node positivity (N1–N3)	18 (69.2%)	12 (33.3%)	0.011*
Grade III tumor	16 (61.5%)	14 (38.9%)	0.029*
Ki-67 >40%	18 (69.2%)	16 (44.4%)	0.031*
BRCA1 mutation	2 (7.7%)	3 (8.3%)	0.91

*Statistically significant (p < 0.05).

DISCUSSION

In our study, the majority of patients were aged 31–35 years, underscoring that TNBC typically appears in early adulthood. Building on this, a systematic analysis of 36 studies indicated that women under 40 diagnosed with TNBC experience greater risks of locoregional and distant recurrence compared to older patients, aligning with the more aggressive disease characteristics observed in younger women [22]. The majority of patients were from urban areas compared to rural locations, highlighting disparities in healthcare access, early detection, and geographic differences

documented in earlier research [23]. Fifty percent of the subjects were homemakers, while the rest were in service, education, or business roles, illustrating regional socio-demographic trends where many breast cancer patients are housewives [24]. In this study of younger TNBC patients, the majority of tumors were classified as T2 (2–5 cm). This corresponds with earlier findings Dent et al., 70%; Ahn et al., 55.5% and 62.8% reported by Nam (2023), indicating that TNBC frequently manifests with tumors exceeding 2 cm, suggesting rapid growth, aggressive characteristics,

and lower histological differentiation [25,26,27].

Lymph node involvement was prevalent, with the majority of patients classified as N1–N3 and one-third being node-negative, aligning with the high nodal metastasis rates and negative prognostic implications of TNBC [28]. The majority of tumors were high-grade (Grade III), aligning with TNBC’s inclination for poor differentiation, increased histological grade, and aggressive characteristics, as documented in several studies [29]. The majority of patients exhibited a noticeable lump, whereas a smaller number experienced pain, skin

alterations, or nipple discharge, illustrating the common presentation of TNBC and frequently advanced local disease [30].

In this younger TNBC group, invasive ductal carcinoma (IDC) was the most common histological type, seen in more than 92% of patients, consistent with global findings by Mohapatra et al. (2023) indicating that IDC of no special type is the prevalent histopathology in TNBC instances [31]. The majority of patients exhibited a high Ki-67 index (>40%), indicating the significant proliferative activity of TNBC. Increased Ki-67 is associated with aggressive tumor behavior, worse prognosis, and might indicate the response to neoadjuvant chemotherapy [32,33]. In Mehrdad Payandeh's research, Ki-67 was not linked to age or tumor grade, yet it showed a correlation with p53 positivity, unlike Keam et al. who reported no association between Ki-67 and p53[34,35]? In the tested subset, BRCA1 mutations were found in 25%, aligning with research that indicates a significant prevalence of BRCA1 alterations in TNBC, especially among younger women, underscoring the importance of genetic predisposition in this subtype [36].

In this research, younger TNBC patients primarily underwent surgery and chemotherapy, with significant number also receiving radiotherapy; however, hormonal and HER2-targeted treatments were not administered. Obidiro et al. (2023) consistently note that the treatment of TNBC depends on chemotherapy and localized therapies because of the absence of targetable receptors, but issues such as resistance, recurrence, and metastasis continue, underscoring the necessity for new therapies [37].

In this younger TNBC group, greater tumor size (T3–T4) and positive lymph nodes (N1–N3) were significantly linked to early relapse, aligning with worldwide studies that connect advanced stage and nodal involvement to increased recurrence risk (Dent et al., 2007) [25].

High-grade III tumors and Ki-67 >40% were linked to early relapse, indicating aggressive TNBC biology; BRCA1 mutation status did not significantly influence early recurrence, aligning with findings that BRCA1 alone might not forecast short-term relapse [38].

CONCLUSION

Younger individuals with triple-negative breast cancer mainly exhibit high-grade, invasive ductal tumors, common lymph node involvement, and aggressive biological characteristics like high Ki-67 and p53 positivity. Conventional treatment depends on surgery, chemotherapy, and radiotherapy since targeted therapies do not work. Premature relapse is closely linked to increased tumor size, positive nodules, high

histological grade, and a heightened proliferation index, underscoring the necessity for vigilant observation and proactive treatment in this high-risk group.

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